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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/626,166	07/23/2003	Gregory Everett Amidon	PC28053	9717

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EXAMINER	
ROGERS, JAMES WILLIAM	

ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
06/06/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/626,166	AMIDON ET AL.	
	Examiner	Art Unit	
	JAMES W. ROGERS	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 04/22/2008 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically claim 1 recites that starch has a specific tensile strength, however tensile strength is an intensive property which means that its value not only depends upon the material itself but also the preparation of the sample (compression forces used to mold tablet for example) and the temperature in which the test was conducted. Applicants have not provided sufficient information within the claimed subject matter for one of ordinary skill in the art to ascertain how the tensile strength was found, thus the claims are unclear and indefinite. It is suggested by the examiner that either the limitation is deleted or applicants amend the claim to include the conditions to make the tablet with the specific tensile strength and the conditions of

the experiment to find the value of the tensile strength. Also it is unclear within claim 1 whether the tensile strength is referring to the entire tablet, the combination of hydrophilic polymer and starch or just starch alone. Further clarification within the claims is required. To expedite the examination process the examiner will search for a tablet with all of the claimed ingredients and the limitation on tensile strength will be considered met if the composition is the same.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4,8-9,13-20 and 24-26 are rejected under 35 U.S.C. 102(e) as being anticipated by Holman (US 6,277,875 B1, cited by applicants).

Holman teaches dopamine D2/D3 receptor agonist for treatment of Fibromyalgia, the treatment can comprise administering pramipexole dihydorchloride monohydrate in the form of MIRAPEX® which contains HPMC and pregelatinized starch, the amount of pramipexole is within applicants claimed ranges. See abstract, col 8 lin 49-57 and col 11 lin 30-46. Regarding the intended use limitation that the tablet is sustained release, Holman teaches the tablets can contain an enteric coating which controls the location in the digestive system where the formulation is released. Furthermore it is noted by the

examiner that applicants have not set forth in their claims any differences in the composition of their claims and the tablets of Holman, thus since the scope of applicants claimed invention and Holman overlap it is inherent that the formulations will have the same release profile. Regarding the limitation on the tensile strength of starch, applicants have not disclosed at least within their claims what feature of the starch would lead to the claimed tensile strength, such as the ratio of amylase/amylopectin or the molecular weights of the two carbohydrate glucoses. Since the only feature that must be present in within the claims is pre-gelatinized starch Holman anticipates applicant's claims. As stated above since this limitation is indefinite with respect to how the starch was compacted and the conditions used to measure the tensile strength the examiner searched for any tablet formulation with the same claimed ingredients, since upon compression with the same forces it is inherent that the same composition will have the same tensile strength. Regarding claims 19-20, Holman teaches that if the composition is in the form of a tablet or capsule it may be coated in a sugar or enteric coating as known in the art. Regarding claim 25 Holman teaches the amount of pramipexole in a MIRAPEX® tablet is 0.125-1.5 mg, and claims a therapeutic amount as low as 0.25 mg per day, therefore it is inherent that one tablet could be used to deliver the therapeutic amount needed in one day. Regarding claim 26 while the Holman patent discloses treating Fibromyalgia with pramipexole the patent also teaches that pramipexole can be used for the treatment of Parkinson's disease. See col 2 lin 48-67.

Claims 1-4,8-4,19-20,22,24 and 26 are rejected under 35 U.S.C. 102(e) as being anticipated by Patel et al. (US 2003/0180352).

Patel teaches solid carriers for improved delivery of active ingredients in pharmaceutical compositions, the active ingredients included anti-Parkinson's drugs such as pramipexole and its salts, the pharmaceutical composition could further comprise a solubilizer such as HPMC (within applicants claimed weight range) and binders such as pregelatinized starch, all of the above can be in the form of a tablet. See abstract, [0052],[0061],[0226]-[0227],[0241],[0272], [0365]. Regarding the limitation on the tensile strength of starch, applicants have not disclosed at least within their claims what features present within their claimed starch would lead to the claimed tensile strength, such as the ratio of amylase/amylopectin or the molecular weights of the two carbohydrate glucoses. Since the only feature that must be present in applicant's claims is pre-gelatinized starch Holman anticipates applicant's claims. As stated above since this limitation is indefinite with respect to how the starch was compacted and the conditions used to measure the tensile strength the examiner searched for any tablet formulation with the same claimed ingredients, since upon compression with the same forces it is inherent that the same composition will have the same tensile strength. Regarding claims 19-20 and 22 Patel discloses that the pharmaceutical composition can be coated with HPMC and ethyl cellulose; also the coating can include an inert-processing aid. See [0273]-[0280].

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-22 and 24-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holman (US 6,277,875 B1) alone or alternatively in view of Michaud et al. (EP 0,933,079 A1, cited previously).

Holman is disclosed above. While Holman discloses using inactive ingredients such as HPMC and pregelatinized starch in MIRAPEX® tablets the patent does not disclose the exact amounts of those inactive ingredients. It is the position of the examiner however that one skilled in the art would through routine experimentation find the optimum amount of fillers, binders and other ingredients to produce a tablet with the desired characteristics such as tablet hardness and release profile. Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969).

As disclosed above Holman is silent on the tensile strength of a tablet of pregelatinized starch although as stated above the reference inherently meets this limitation. However, alternatively this limitation is also obvious when Holman is combined with the Michaud reference below.

Michaud is used only to show that pregelatinized starch was already known to have tensile strength within applicants claimed amounts when compressed into a tablet form. See tables 3,6,9-13. The pregelatinized starch of Michaud was said to produce

very hard tablets at low compression rates. See [0025]. Thus it would have been obvious to one of ordinary skill in the art at the time of applicants claimed invention to substitute/modify the pregelatinized starch of Holman for the pregelatinized starch of Michaud and have a reasonable expectation of success since the two ingredients are essentially the same and the substitution would not materially alter the composition of Holman. One of ordinary skill in the art would have been motivated to combine the two references in order to achieve the disclosed advantages of the starches described in Michaud which produced hard tablets at low compression rates a feature that would obviously be an advantage for the industrial production and processability of the tablet.

Claims 1-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Patel et al. (US 2003/0180352) alone or alternatively in view of in view of Michaud et al. (EP 0,933,079 A1, cited previously).

Patel is disclosed above. While Patel discloses tablets comprised of pramipexole, HPMC and pregelatinized starch the patent does not disclose the amount in weight % compared to the overall weight of the tablet of pregelatinized starch and the coating, the amount of pramipexole and the ratio of ethylcellulose or water-insoluble component and HPMC used in the coating. It is the position of the examiner however that one skilled in the art would through routine experimentation find the optimum amount of fillers, binders, coatings, ratio of ingredients in the coating to produce a tablet with the desired characteristics such as hardness and release profile. Furthermore the case laws of In re Aller and In re Hoeschele above are incorporated herein.

As disclosed above Patel is silent on the tensile strength of a tablet of pregelatinized starch although as stated above the reference inherently meets this limitation. However, alternatively this limitation is also obvious when Patel is combined with the Michaud reference below.

Michaud is used only to show that pregelatinized starch was already known to have tensile strength within applicants claimed amounts when compressed into a tablet form. See tables 3,6,9-13. The pregelatinized starch of Michaud was said to produce very hard tablets at low compression rates. See [0025]. Thus it would have been obvious to one of ordinary skill in the art at the time of applicants claimed invention to substitute/modify the pregelatinized starch of Patel for the pregelatinized starch of Michaud and have a reasonable expectation of success since the two ingredients are essentially the same and the substitution would not materially alter the composition of Patel. One of ordinary skill in the art would have been motivated to combine the two references in order to achieve the disclosed advantages of the starches described in Michaud which produced hard tablets at low compression rates a feature that would obviously be an advantage for the industrial production and processability of the tablet.

Claims 1-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holman (US 6,277,875 B1, cited by applicants) in view of Khan et al. (US 5,656,296, cited by applicant) in view of Petrus et al. (WO 00/59477 A1, cited by applicants) in further view of Michaud et al. (EP 0,933,079 A1, cited by applicants).

Holman is disclosed above. While Holman discloses using inactive ingredients such as HPMC, pregelatinized starch and coating the tablets, the patent does not disclose the exact amounts of those inactive ingredients nor does the patent disclose the use of a coating comprising a water-insoluble component and HPMC within the ratio specified by applicant in claim 23.

Khan is used to primarily show that a coating comprised of a water-insoluble component and HPMC-based pore forming component within the ratio to each other and weight percent of the overall tablet as claimed by applicant was well known at the time of the invention to be useful in sustained release drug delivery systems. See abstract and col 6 lin 34-col 7 lin 17. Khan also disclosed that the coating can contain conventional excipients and additives which function to facilitate processing or storage. Khan disclosed the sustained release formulations were not effected by the consumption of food which is a known problem in pharmaceuticals containing water soluble drugs which are known to be rapidly released in the blood system due to the consumption of food. Thus since Khan and Holman are related, at least as coated tablet formulations one of ordinary skill in the art would have a reasonable expectation of success in using the coating of Khan and substituting it for the coating of Holman. The advantage of using the coating of Khan would be that pramipexole dihydorchloride would not be affected by consumption of food which in other types of formulations resulted in immediate release of the water soluble active.

Petrus is used to show that the amount of HPMC and pregelatinized starch within the weight percent of the overall tablet specified by applicant was well known in the art

at the time of the invention for use in controlled release formulations for Parkinson's disease. See abstract and pag 20 lin 21-37. Thus since both Holman and Petrus are related to the same filed of endeavor one of ordinary skill in the art would have a reasonable expectation of success in using the amounts of HPMC and pregelatinized starch of Petrus and substituting those amounts within Holman who also teaches the use of HPMC and pregelatinized starch. Thus the claimed invention would have been *prima facie* obvious since all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Michaud is used only to show that pregelatinized starch was already known to have tensile strength within applicants claimed amounts when compressed into a tablet form. See tables 3,6,9-13. The pregelatinized starch of Michaud was said to produce very hard tablets at low compression rates. Thus it would have been obvious to one of ordinary skill in the art at the time of applicants claimed invention to substitute/modify the pregelatinized starch of Holman for the pregelatinized starch of Michaud and have a reasonable expectation of success since the two ingredients are essentially the same and the substation would not materially effect the composition of Holman. One of ordinary skill in the art would have been motivated to combine the two references in order to achieve the disclosed advantages of the starches described in Michaud which produced hard tablets at low compression rates, a feature that would obviously be advantageous in industrial production and processability of the tablet.

Response to Arguments

Applicant's arguments filed 04/22/2008 have been fully considered but they are not persuasive.

Applicants assert that Holman fails to disclose a sustained release formulation and MIRAPEX and REQUIP cited within the reference are immediate release drugs as shown by the PDR cited by applicants. Applicants further assert that the tensile strength cannot be considered an inherent property of the starch and that tensile strength can vary among starch samples.

The examiner respectfully disagrees with the above assertion by applicants. Firstly as noted in the rejection above Holman does describe the use of an enteric coating, it is well known by artisans ordinary skill that an enteric coating is used to control the release of a pharmaceutical within the digestive tract, thus clearly Holman does not just teach immediate release forms as suggested by applicants. Secondly as already mentioned by the examiner there is no patentable distinction within applicants claims that would preclude the tablet of Holman, since the two compositions are essentially the same it is inherent that the ingredients will have the same release properties and tensile strength. It is also noted by the examiner that the cited Michaud reference teaches pregelatinized starch, particularly the commercially available Starch 1500 which has a tensile strength greater than applicant's claimed lower limit. Thirdly as mentioned in the 112 2nd paragraph rejection the examiner had to conduct his search for what was clearly claimed, that is the ingredients claimed that are present within a tablet

formulation. Since tensile strength is an intensive property and would depend on the methods to produce the tablet (compression force) and temperature the tensile strength was measured it is not possible for the examiner to search for this limitation since it is not known with certainty the parameters used to measure the value.

Applicants also assert that Patel also does not inherently teach the claimed tensile strength.

As stated above since commercially available starches have a tensile strength greater than applicants claimed lower limit the limitation is considered met. Also the remarks on indefiniteness and how the claims were searched are incorporated herein.

Applicants lastly assert in regards to the 35 USC 103(a) rejection over Holman, Khan, Petrus and Michaud fail to teach or suggest all of the claimed limitations. Applicants assert that since both Holman and Michaud are drawn to immediate release formulations there would be no reasonable expectation of success to arrive at applicants claimed sustained release formulation.

The examiner respectfully disagrees with the above assertions by applicants. Clearly as noted above Holman does teach other types of formulations besides immediate release compositions. Furthermore applicants have not described where within the Michaud reference it states that all tablet forms described within are immediate release. Even if for the sake of argument the above is true, Michaud was only used for its description of the tensile strength of various starches and as a secondary reference it does not have to disclose all of applicants claimed invention.

Conclusion

No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to James W. Rogers, Ph.D. whose telephone number is (571) 272-7838. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Michael G. Hartley/

Supervisory Patent Examiner, Art Unit 1618